

WHAT IS CLAIMED IS:

1. A method of creating a chemical compound library comprising:
selecting compounds having a molecular weight of no greater
5 than about 350 grams/mole; and
selecting compounds having a solubility in deuterated water of at
least about 1 mM at room temperature.
2. The method of claim 1 wherein a majority of the compounds in the
10 chemical compound library have a molecular weight of no greater than
about 350 grams/mole and a solubility in deuterated water of at least
about 1 mM at room temperature.
3. The method of claim 2 wherein all of the compounds in the chemical
15 compound library have a molecular weight of no greater than about 350
grams/mole and a solubility in deuterated water of at least about 1 mM at
room temperature.
4. The method of claim 1 wherein the compounds selected have a molecular
20 weight of no greater than about 325 grams/mole.
5. The method of claim 4 wherein the compounds selected have a molecular
weight of less than about 325 grams/mole.
- 25 6. A chemical compound library comprising compounds having a molecular
weight of no greater than about 350 grams/mole and a solubility in
deuterated water of at least about 1 mM at room temperature.
7. The library of claim 6 wherein a majority of the compounds have a
30 molecular weight of no greater than about 350 grams/mole and a
solubility in deuterated water of at least about 1 mM at room
temperature.
8. The library of claim 7 wherein all of the compounds have a molecular

weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.

9. The library of claim 6 wherein the compounds have a molecular weight
5 of no greater than about 325 grams/mole.
10. The library of claim 9 wherein the compounds have a molecular weight
of less than about 325 grams/mole.
- 10 11. A method of identifying a lead chemical template, the method
comprising:
selecting compounds having a molecular weight of no greater
than about 350 grams/mole and a solubility in deuterated water of at least
about 1 mM at room temperature to create a chemical compound library;
15 identifying at least one compound from the library that functions
as a ligand to a target molecule having a dissociation constant of at least
about 100 μ M; and
using the ligand to identify a lead chemical template.
- 20 12. The method of claim 11 wherein a majority of the compounds in the
chemical compound library have a molecular weight of no greater than
about 350 grams/mole and a solubility in deuterated water of at least
about 1 mM at room temperature.
- 25 13. The method of claim 12 wherein all of the compounds in the chemical
compound library have a molecular weight of no greater than about 350
grams/mole and a solubility in deuterated water of at least about 1 mM at
room temperature.
- 30 14. The method of claim 11 wherein the compounds selected for the library
have a molecular weight of no greater than about 325 grams/mole.
15. The method of claim 14 wherein the compounds selected for the library

have a molecular weight of less than about 325 grams/mole.

16. The method of claim 11 wherein the dissociation constant of a lead chemical template to the target molecule is at least about 1 μ M.
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17. The method of claim 11 wherein the target molecule is a protein.
18. A method of identifying a compound that binds to a target molecule, the method comprising:
- 10 providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;
- introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;
- providing a nuclear magnetic resonance spectrometer equipped
- 15 with a flow-injection probe;
- transferring each test sample from the sample reservoir into the flow-injection probe;
- collecting a relaxation-edited nuclear magnetic resonance spectrum on each sample in each reservoir; and
- 20 comparing the spectra of each sample to the spectra taken under the same conditions in the absence of the target molecule to identify compounds that bind to the target molecule;
- wherein the concentration of target molecule and each compound in each sample is no greater than about 100 μ M.
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19. The method of claim 18 wherein each mixture is in a sample reservoir of a multiwell sample holder.
20. The method of claim 19 wherein the multiwell sample holder is a 96-well
- 30 microtiter plate.
21. The method of claim 18 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.

22. The method of claim 18 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.
- 5 23. The method of claim 18 wherein collecting a relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited nuclear magnetic resonance spectrum.
24. The method of claim 23 wherein collecting a 1D relaxation-edited
10 nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited ^1H nuclear magnetic resonance spectrum.
25. The method of claim 18 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable
15 resonance in a 1D NMR spectrum of the mixture.
26. The method of claim 25 wherein the mixture of compounds comprises at least about 6 compounds.
- 20 27. The method of claim 25 wherein the ratio of target molecule to each test compound in each sample reservoir is about 1:1.
28. The method of claim 18 wherein the concentration of target molecule and each compound in each sample is no greater than about 50 μM .
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29. The method of claim 18 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100 μM .
30. The method of claim 18 wherein the target molecule is a protein.
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31. A method of identifying a compound that binds to a target molecule, the method comprising:
providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;

introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

providing a nuclear magnetic resonance spectrometer equipped with a flow-injection probe;

5 transferring each test sample from the sample reservoir into the flow-injection probe;

collecting a WaterLOGSY nuclear magnetic resonance spectrum on each sample in each reservoir; and

10 analyzing the spectra of each sample to distinguish binding compounds from nonbinding compounds by virtue of the opposite sign of their water-ligand NOEs.

32. The method of claim 31 wherein the concentration of target molecule is no greater than about 10 μ M.

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33. The method of claim 32 wherein the concentration of target molecule is no greater than about 1 μ M.

34. The method of claim 31 wherein the concentration of each compound in
20 each sample is no greater than about 100 μ M.

35. The method of claim 31 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.

25 36. The method of claim 31 wherein each mixture is in a sample reservoir of a multiwell sample holder.

37. The method of claim 36 wherein the multiwell sample holder is a 96-well microtiter plate.

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38. The method of claim 31 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.

39. The method of claim 38 wherein each test compound has a molecular weight of no greater than about 325 grams/mole.
40. The method of claim 31 wherein collecting a WaterLOGSY nuclear magnetic resonance spectrum comprises collecting a 1D WaterLOGSY nuclear magnetic resonance spectrum.
41. The method of claim 31 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable resonance in a 1D NMR spectrum of the mixture.
42. The method of claim 41 wherein the mixture of compounds comprises at least about 6 compounds.
43. The method of claim 31 wherein the ratio of target molecule to each test compound in each sample reservoir is about 100:1 to about 10:1.
44. The method of claim 31 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100 μ M.
45. The method of claim 31 wherein the target molecule is a protein.